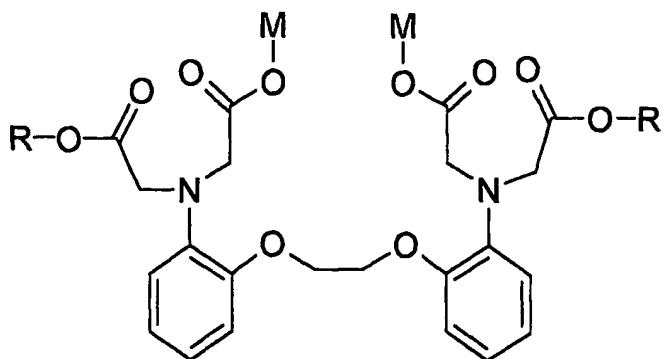


CLAIMS:

1. A method of inhibiting protease activity, said protease being selected from metalloproteinase and calpain, the method comprising exposing cells to inhibiting amount of a compound of the general formula (I):

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(I)



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any

10 combination of 1-6 oxygen and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and M denotes a hydrogen or a physiologically acceptable cation.

2. The method according to claim 1 wherein R is a phenylalkyl.

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3. The method according to claim 1 wherein R is an alkyl interrupted by zero to three oxygen atoms.

4. The method according to claim 1 wherein R is a monoalkyl ether of mono-, di-, or tri-ethylene glycol.

20 5. The method according to claim 1 wherein R is selected from the group consisting of: C₈H₁₇, C₈H₁₇OCH₂CH₂, C₁₈H₃₇, C₁₈H₃₇OCH₂CH₂, benzyl-CH₂OCH₂CH₂, C₁₂H₂₅OCH₂CH₂, C₁₂H₂₅(OCH₂CH₂)₂ and C₁₂H₂₅(OCH₂CH₂)₃.

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6. The method according to claim 1, wherein said protease is a matrix metalloproteinase (MMP).
7. The method according to claim 6, wherein the matrix metalloproteinase 5 is MMP-9.
8. The method according to claim 1, wherein said protease is a calpain.
9. A method for preventing, treating or managing a MMP-related disease 10 or disorder in a mammal comprising administering to a mammal in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of a compound of the general Formula (I).
10. A method for preventing, treating or managing a calpain-related disease 15 or disorder in a mammal comprising administering to a mammal in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of a compound of the general Formula (I).
11. The method according to claim 9 or 10, wherein said method further 20 comprises treating the mammal with additional therapeutic treatment.
12. The method according to any one of claims 9 to 11, wherein said mammal is a human.
- 25 13. The method according to claim 9 or 10, wherein said MMP- or calpain-related disease or disorder is selected from the group consisting of cancer, stroke, trauma, inflammatory conditions and diseases, atherosclerosis, thrombotic disorders, arthritis, hemorrhage, rheumatic diseases, autoimmune diseases, neurological diseases and disorders, migraine, cerebrovascular and 30 cardiovascular disorders.

14. The method according to claim 13, wherein said inflammatory conditions and diseases are selected from the group consisting of arthritides, rheumatoid arthritis, osteoarthritis, restenosis, asthma, psoriasis, systemic lupus erythematosus, inflammatory bowel syndrome, Crohn's disease, migraine, 5 gingivitis, periodontitis, meningitis, tropical spastic paraparesis, sepsis, bullous skin disorders, acne and inflammation due to infectious diseases.

15. The method according to claim 9 or 10, wherein said MMP- or calpain-related disease or disorder is selected from the group consisting of ischemic or 10 hypoxic tissue damage, oxidative damage, osteoporosis, diabetes, hemorrhage, ocular pathologies and retinopathies, diabetic retinopathy, glaucoma, macular degeneration, cataract, retinal detachment and retinal tears.

16. The method according to claim 9 or 10, wherein said MMP- or calpain-related disease or disorder is selected from the group consisting of 15 neurodegenerative diseases or disorders, multiple sclerosis (MS), Alzheimer's disease (AD), motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), Guillain-Barré, Parkinson's disease, Huntington disease, Pick's disease, dementia syndrome, vascular dementia, multiple infarct dementia, HIV-induced neural disorders, brain ischemia (both global and focal ischemia) and 20 neuronal tissue trauma.

17. A method for preventing, treating or managing cancer associated with increased activity of metalloproteinase comprising administering to a patient in 25 need thereof a pharmaceutical composition comprising a therapeutically effective amount of a compound of the general Formula (I).

18. A method according to claim 17, wherein said cancer includes cancer metastasis.

19. A method for treating a patient suffering from an angiogenesis-dependent disease comprising administering to said patient a pharmaceutically effective amount of a compound of the general Formula (I).

5 20. The method according to claim 19, wherein said angiogenesis-dependent disease is selected from cancerous tumors, arthritis, psoriasis, macular degeneration, chronic inflammation and diabetic retinopathy.

10 21. The method according to any one of claims 17 to 19, wherein said method further comprises treating the patient with additional therapeutic treatment.

15 22. The method according to claim 21, wherein said additional treatment is selected from chemotherapy, irradiation therapy, immunotherapy, genetic therapy and surgery.

20 23. The method according to claim 21, wherein said additional treatment is carried out concurrently with the administration of the pharmaceutical composition comprising a compound of the general Formula (I).

24. The method according to claim 21, wherein said additional treatment is preceding the administration of the pharmaceutical composition comprising a compound of the general Formula (I).

25 25. The method according to claim 21, wherein said additional treatment is subsequent to the administration of the pharmaceutical composition comprising a compound of the general Formula (I).

30 26. The method according to any one of claims 9 to 25, wherein said compound of the general formula I is selected from the group consisting of

1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octoxyethyl acetate), N,N'-diacetic acid;

1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octodecyloxyethyl acetate), N,N'-diacetic acid;

5 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-benzyloxyethyl acetate), N,N'-acetic acid;

1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-dodecyloxyethyl acetate), N,N'-diacetic acid;

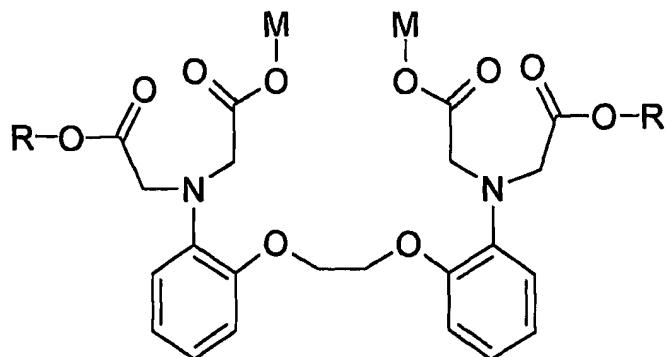
10 1,2-bis(2-aminophenoxy)ethane, N,N'-di[2-(2-dodecyloxyethoxy)-ethyl acetate], N,N'-diacetic acid; and

1,2-bis(2-aminophenoxy)ethane, N,N'-di{2-[2-(2-dodecyloxyethoxy)ethoxy]-ethyl acetate}, N,N'-diacetic acid.

27. Use of a compound of the general formula (I):

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(I)



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other;

20 and M denotes a hydrogen or a physiologically acceptable cation, for the preparation of a medicament for inhibiting the activity of a protease selected from metalloproteinase and calpain.

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28. The use according to claim 27, wherein said compound of the general formula (I) is selected from the group consisting of
1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octoxyethyl acetate), N,N'-diacetic acid;

5 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octodecyloxyethyl acetate), N,N'-diacetic acid;

1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-benzyloxyethyl acetate), N,N'-acetic acid;

10 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-dodecyloxyethyl acetate), N,N'-diacetic acid;

1,2-bis(2-aminophenoxy)ethane, N,N'-di[2-(2-dodecyloxyethoxy)-ethyl acetate], N,N'-diacetic acid; and

15 1,2-bis(2-aminophenoxy)ethane, N,N'-di{2-[2-(2-dodecyloxyethoxy)ethoxy]-ethyl acetate}, N,N'-diacetic acid.

29. The use according to claim 27, wherein the medicament is for the treatment of MMP- or calpain-related disease or disorder selected from the group consisting of cancer (including metastasis cancer), ischemic or hypoxic tissue damage, oxidative damage, stroke, trauma, inflammatory conditions and

20 diseases, hemorrhage, rheumatic diseases, autoimmune diseases, neurological diseases and disorders, cardiovascular disorders, cerebrovascular and neurodegenerative diseases and disorders.

30. A compound of the general formula (I) which is 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-benzyloxyethyl acetate), N,N'-acetic acid.

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31. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 30 and a pharmaceutically acceptable carrier or excipient.

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